

Mydriatic drugs for diabetic patients

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SUMMARY A comparative study in healthy subjects and diabetic patients of the mydriatic response to topical tropicamide 0.5% with and without added phenylephrine 10% is reported. The findings indicate that diabetic pupils respond relatively poorly to tropicamide alone but adequately and completely to the drug combination. The pupils of diabetic patients whose eyes had previously received laser treatment dilated less than those from untreated eyes by a small but significant extent. This combination of drugs is recommended for all diabetic patients to provide an adequate mydriasis with a minimum of postclinic accommodative paralysis.

It is well known that the diabetic pupil dilates poorly to standard anticholinergic eye drops.¹ This often results in application of excessive dosage of the more powerful agents such as cyclopentolate and homatropine, which leaves visual accommodation paralysed for several days.² The finding that the sympathetically denervated small pupil of diabetic patients is supersensitive to sympathomimetics^{3,4} suggests an alternative approach. A combination of the sympathomimetic phenylephrine to ensure adequate dilatation with the rapidly acting anticholinergic tropicamide⁵ to abolish the light reflex should provide a regimen to which the diabetic pupil is particularly sensitive with the minimum accommodative loss. This study has tested the efficacy of this combination in normal persons and diabetic patients, half of whom had previously undergone laser treatment for proliferative retinopathy.

Material and methods

Twenty healthy subjects (13 male, 7 female) aged 31-62 years and 41 diabetic patients (22 male, 19 female) aged 17-70 years voluntarily took part in the investigation. Many of the patients, who were unselected for type or treatment of diabetes, had diabetic eye disease and were attending the Department of Ophthalmology for observation and/or treatment of retinopathy. Twenty-four of these patients had previously received argon laser photocoagulation treatment to one or both eyes.

Pupil diameters were measured in the dark and under continuous bright illumination by infrared

television pupillography.⁶ This illumination, from two strip lamps placed 50 cm from the patient, was of an intense brightness comparable to that needed for ophthalmic practice. Pupils were measured before and after application of mydriatic eyedrops: tropicamide 0.5% and phenylephrine 10% (Minims, Smith and Nephew Pharmaceuticals).

Two mydriatic regimens were tested. In the first regimen 2 drops of tropicamide alone were given to one eye of all the subjects, and the peak effects were measured 30 min after instillation. Pilot experiments had shown that light reflex inhibition had reached a maximum at that time in all subjects. In the second regimen the same application of tropicamide was preceded by instillation of 2 drops of phenylephrine 30 min previously. This timing was chosen because the peak mydriatic effects of phenylephrine are reached in about twice the time taken by tropicamide.^{5,7} This regimen was tested in 14 healthy and 33 diabetic subjects. As with the first regimen, measurements were made 30 min after tropicamide.

The results of the experiments were evaluated by standard statistical methods. There was no significant age difference between the three groups studied (normals, diabetic patients with and without laser treatment) within or between the two drug regimens. The study received ethical approval from the Research (Endowments) Committee of West Lambeth Health Authority.

Results

Pupil diameters before and after each treatment are illustrated in Fig. 1. Before instillation of mydriatics the diabetic pupils were smaller in darkness than the

healthy pupils ($p < 0.001$) and those of eyes with previous laser treatment smaller than those without ($p < 0.001$). Under bright light the pupils of diabetics were no smaller than those of healthy subjects, irrespective of prior laser treatment. Thus prior to eye drops the difference in size between the diabetic and the healthy pupil was apparent only when measured in darkness.

After tropicamide alone the diabetic pupils dilated to a smaller final diameter than the healthy pupils ($p < 0.001$), the difference being greater in those eyes previously exposed to laser treatment ($p < 0.001$). Thus the healthy pupils dilated to 7.59 ± 0.18 mm (mean \pm SEM), those from the untreated diabetic eyes to 6.58 ± 0.17 mm, and those from the laser-treated eyes to only 5.88 ± 0.21 mm.

After phenylephrine plus tropicamide the pupil diameters were larger than after tropicamide alone in all subjects. Diabetic pupils of eyes not exposed to laser treatment dilated to the same final diameter as healthy pupils (7.99 ± 0.16 mm and 8.21 ± 0.17 respectively). Those of eyes previously exposed to laser treatment dilated to a slightly smaller mean diameter of 7.53 ± 0.19 mm ($p < 0.05$). In all diabetic patients the increment in diameter produced by addition of phenylephrine to the tropicamide treatment was significantly greater than in healthy subjects.

Small light reflex responses to illumination were

observed in some (particularly the healthy) subjects following both mydriatic regimens (Table 1). These residual responses to the intense light stimulation used were always minimal and were insignificant in the diabetic patients tested with the combination regimen.

Multiple regression analysis showed that the final pupillary diameters after either regimen in healthy and diabetic subjects were uninfluenced by age, sex, or eye colour differences.

Discussion

This study has shown that the diabetic pupil fails to dilate normally to darkness, particularly in those eyes previously treated with laser photocoagulation. This failure of dilatation has been shown to be due, at least in part, to a sympathetic dysfunction related to the autonomic neuropathy of these patients.⁴ The diabetic pupil also failed to dilate adequately to tropicamide eye drops. The addition of phenylephrine, which utilises the denervation supersensitivity of the small diabetic pupil, greatly improved the mydriatic drug response in diabetic patients. Quantitatively this improvement averaged 1.41 mm and 1.65 mm in the untreated and laser-treated eyes respectively and thus is of great value clinically.

Tropicamide 0.5% was effective at 30 min in

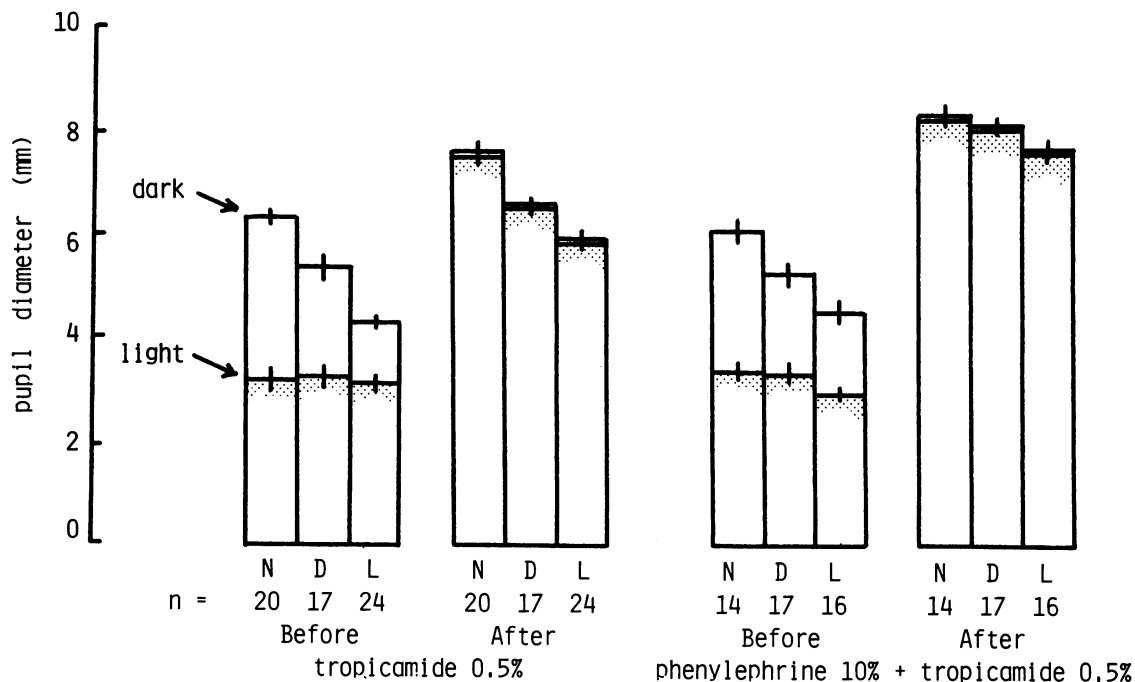


Fig. 1 Pupil diameters in darkness and in light before and after instillation of mydriatic eyedrops. N=healthy subjects; D=diabetic eyes without laser treatment; L=diabetic eyes with prior laser treatment.

Table 1 Numbers of healthy and diabetic subjects with residual light responses (mm) after instillation of tropicamide 0.5% or phenylephrine 10% + tropicamide 0.5%

	Total n	Response (mm)						p*
		0-0.1	<0.2	<0.3	<0.4	<0.5	<0.6	
Tropicamide								
Healthy	20	11	3	1	1	1	3	<0.01
Diabetic	41	30	5	5	1			<0.05
Phenylephrine + tropicamide								
Healthy	14	10	3	0	0	1		<0.05
Diabetic	33	25	6	2				NS

*Significance of difference of group mean from zero.

antagonising the light reflex response to the intensely bright light used, which was comparable to the intensity of light necessary in ophthalmic practice. This fast-acting anticholinergic drug was preferred to stronger agents such as cyclopentolate or homatropine to avoid the prolonged accommodative paralysis that occurs with these agents. There were no reports of subjective discomfort with either regimen. As neither glare nor accommodative problems occurred, we did not consider reversal with miotic drops, which can themselves cause discomfort.

Our findings do, however, indicate that pupils of diabetic patients who have had laser treatment for proliferative retinopathy are especially difficult to dilate, even with the combined mydriatic regimen. It is known that the pupillary signs of diabetes are more marked in patients with proliferative compared with background retinopathy.³ Thus it is not clear whether laser treatment per se, or a more advanced stage of diabetic eye disease, makes the pupil more resistant to mydriatics. However, from the practical point of view the combination regimen did satisfactorily dilate the pupil to 7.5 mm in the light in these laser-treated eyes.

In conclusion, the combination of phenylephrine and tropicamide provides a very effective and comfortable mydriasis for fundal inspection in the diabetic patient.

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